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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,568	10/09/2003	Daniel Buttry	51830.12.5	6818

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/681,568	BUTTRY ET AL.
	Examiner	Art Unit
	Vera Afremova	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2006*.
2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.
  4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-15* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
  Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
  Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5 as amended and new claims 6-15 (filed 3/14/2006) are pending and under examination.

Claim Rejections - 35 USC § 112

Claim 4 as amended and new claims 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 as amended now recites the use of "particulates" that are potentially or optionally intended to interact with "a chemical agent" and/or to affect background fluorescence. Thus, it is unclear whether "particulates" are required to be within the claimed aqueous sample. Therefore, the components of the composition as claimed cannot be determined. Applicant's definitions of "particulates" are rather vague and encompass unidentified debris including generic minerals (page 6, lines 24-25).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4 as amended and new claims 6 and 11 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,221,612 (Knapp et al.) as explained in the prior office action and for the reasons below.

Claims 1 and 4 as amended and new claims 6, 8, 11 and 13 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,221,612 (Knapp et al.) or by US 5,582,982 (Cubbage et al.) as explained in the prior office action and for the reasons below.

Claims are directed to a method for reducing background fluorescence comprising steps of labeling cells in a solution with a fluorescent agent that is permeant to the cells and contacting the solution with a chemical agent that modifies extracellular fluorescent agent, thus, reducing background fluorescent of the solution by at least 10%. Some claims are directed to an aqueous sample comprising cells labeled with the fluorescent agent and the chemical agent.

Some claims are/are further drawn to the presence in the solution of "particulates" including minerals in the method for reducing background fluorescence in the solution. Some claims are further drawn to the use of a fluorescent agent comprising a nucleic acid probe in the method for reducing background fluorescence.

US 6,221,612 (Knapp et al.) discloses a method for reducing background fluorescence comprising step of loading cells suspended in a solution with a fluorescent probe that is a photon producing agent and step of adding to the solution a chemical agent (a photon reducing agent) that modifies the fluorescent probe by reducing photon (example 7, col. 35-36). The cited patent teaches that the background fluorescent is reduced (col. 35, lines 32-33 and col. 36, lines 36-39) and that the reading of the cell-based assays is improved at least by 200-300 % (col. 35, line 57). The method for reducing background fluorescence of the cited patent encompasses measuring fluorescence in solution comprising unwashed cells and, thus, the solution inherently comprises at least some debris and/or minerals that are "particulates" within the meaning of the instant invention (page 6, lines 24-25).

US 5,582,982 (Cubbage et al.) discloses a method for reducing background fluorescence comprising step of labeling cells in a solution with fluorescein as a fluorescent agent that is permeant to the cells and contacting the solution with chemical agent or dye that modifies extracellular fluorescent agent, thus, reducing background fluorescent of the solution. The method for reducing background fluorescence of the cited patent encompasses the use of fluorescent agent comprising a nucleic acid probe (col. 9, lines 59-64, for example). The method for reducing background fluorescence of the cited patent encompasses measuring fluorescence in solution comprising buffer or PBS (col. 10, line 37, for example) and, thus, the solution inherently comprises at least some "mineral particulates" within the meaning of the instant invention (page 6, lines 24-25).

Thus, the cited patents disclose identical methods and aqueous samples and, therefore, anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 as amended and new claims 6-15 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,221,612 (Knapp et al.) and/or US 5,582,982 (Cubbage et al.) taken with Aldrich Catalogue (Aldrich Handbook of Fine Chemicals and Laboratory Equipment.

2000-2001, pages 28 and 121) and Kano et al. (Journal of Physical Chemistry, (1983), Vol. 87, No. 4, pages 566-569) as explained in the prior office action and for the reasons below.

Claims are directed to a method for reducing background fluorescence comprising steps of labeling cells in a solution with a fluorescent agent that is permeant to the cells and contacting the solution with a chemical agent that modifies extracellular fluorescent agent, thus, reducing background fluorescent of the solution by at least 10%. Some claims are directed to an aqueous sample comprising cells labeled with the fluorescent agent and the chemical agent. Some claims are further drawn to the use of acid black 48 as a chemical agent that modifies extracellular fluorescent agent and, thus, reduces background fluorescent.

Some claims are/are further drawn to the presence in the solution of "particulates" including minerals in the method for reducing background fluorescence in the solution. Some claims are further drawn to the use of a fluorescent agent comprising a nucleic acid probe in the method for reducing background fluorescence.

US 6,221,612 (Knapp et al.) and/or US 5,582,982 (Cubbage et al.) are relied upon as explained above for the disclosure of methods for reducing background fluorescence in the cell-based assays wherein chemical agents are used to modify extracellular fluorescent agent to reduce the background fluorescent. In particular disclosure of the cited patent US 5,582,982 (Cubbage et al.) the method for reducing background fluorescence comprises the use of fluorescent agent attached to a nucleic acid probe (examples 1-2). Although in a particular example the cited US 6,221,612 (Knapp et al.) discloses an enzyme based fluorescent agent, it clearly suggests the use of fluorescent agent with nucleic acid probe by teaching that test targets include both enzyme and nucleic acids (col. 15, lines 40-45).

The cited patents US 6,221,612 (Knapp et al.) and US 5,582,982 (Cubbage et al.) are lacking particular teaching about the use of acid black 48 for reduction of background fluorescence.

However, US 5,582,982 (Cubbage et al.) suggests that dyes suitable for reduction of background fluorescence have polyaromatic moiety and amino group (col. 6, lines 61-65). The dye acid black 48 has polyaromatic moiety and amino group as shown on page 28 of Aldrich Catalogue.

US 6,221,612 teaches that the chemical agents suitable for reduction of background fluorescence include photon reducing compounds that have absorption spectrum overlapping with the absorption, excitation or emission spectrum of a fluorescent agent or a photon producing agent applied in the assays and that photon reducing agents quench photon-producing agents. The cited reference by Kano et al. teaches that anthraquinone compounds provide for fluorescence quenching (entire document including title) and the Aldrich Catalogue demonstrates that Acid black 48 is an anthraquinone compound (page 28 and 121) and, thus, could provide for fluorescence quenching.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use chemical agent(s) such as acid black 48 with a reasonable expectation of success in reducing background fluorescence in the cell-based fluorescence assays because acid black 48 is an anthraquinone compound providing for fluorescence quenching and having chemical structures similar to chemical agents suitable for reduction of background fluorescence as adequately taught and/or suggested by the prior art for a generic fluorescent agent. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 3/14/2006 have been fully considered but they are not persuasive.

Main argument is directed to the idea that the cited patents alone or in combination do not teach and/or suggest presence of "particulates" in assay solution and reducing the fluorescence of fluorophore associated with the "particulates" present in the assay solution. However, the Applicant's definitions of "particulates" are rather vague and encompass some unidentified debris including generic minerals (page 6, lines 24-25).

With regard to US 6,221,612 (Knapp et al.) applicants argue that Knapp et al. provide such definitions of "solution fluorescence" (col. 8, lines 24-34) that exclude fluorophore adsorbed on "particulates" as the target for the photon reducing agent. Upon review it is not found particularly true because "solution fluorescence" encompasses fluorophore association with "test compound" in an assay "buffer". Given broadest interpretation, both terms including "test compound" and "buffer" fall within generic meaning of the applicants' "particulates" that are some unidentified compounds or debris including generic minerals. Applicants further argue that Knapp et al. actually states that some "particulates" can act beneficially as photon reducing agents (i.e. as quenchers) by scattering away the undesirable solution fluorescence (col. 11, lines 1-3 and col. 31, lines 3-5). Yet, Knapp et al. does not define what are those "particulates" can act beneficially as photon reducing agents to consider some potential teaching away, is any. In particular example (col. 31, lines 14-16) the Knapp's "particulates" acting as photon reducing agents appear to be diatrizoic acid and Higgins ink that are neither disclosed nor claimed by the instant invention. Thus, generic term "particulates" have different meaning as disclosed by Knapp et al. and as intended for the present invention. Moreover, the method for reducing background fluorescence of the cited patent US 6,221,612 (Knapp et al.) encompasses measuring fluorescence in solution comprising unwashed cells (col. 36, lines 36-37) and, thus, the solution inherently comprises at least some debris and/or minerals that are "particulates" within the meaning of the instant invention.

With regard to US 5,582,982 (Cubbage et al.) applicants argue that Cubbage et al actually requires that the cells be removed from the fluorescent probe solution prior to analysis (col. 2, lines 50-60 and col. 4, lines 12-16) and, therefore, the cited patent does not disclose reducing fluorescence in solution or on "particulates" because any labeled "particulates" would be left behind in the labeling solution when the cells are removed. This argument is not found convincing in the light of vague and broad definitions the applicants' "particulates". The method for reducing background fluorescence of the cited patent US 5,582,982 encompasses measuring fluorescence in solution comprising some components of wash solution and PBS (col. 10, line 35-37, for example) and, thus, the test solution comprises at least some "mineral particulates" within the meaning of the instant invention.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

May 26, 2006

V. Afremova

VERA AFREMOVA

PRIMARY EXAMINER